

Case report

Near fatal eosinophilic gastroenteritis responding to oral sodium chromoglycate

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SUMMARY Eosinophilic gastroenteritis (EG) is an uncommon disorder, characterised by cramping abdominal pain, diarrhoea and vomiting and histologically by eosinophilic infiltration of bowel wall.¹ We present a patient who developed EG during the course of a systemic, necrotising vasculitis, who became critically ill after failure of treatment with corticosteroids and cytotoxic drugs and responded only to oral sodium chromoglycate.

Case report

A 57 years old cachectic woman was admitted as an emergency, with a five months history of increasing epigastric pains, anorexia, bloody diarrhoea, and weight loss.

Ten years earlier, she had been diagnosed as having a sero negative, non-erosive, symmetrical polyarthrititis. A year before this admission she was investigated for a painful peripheral neuropathy, livedo reticularis skin rash and leg ulcers. Non-specific vasculitis was present on a skin biopsy. Thereafter she became generally unwell developing mild diarrhoea with weight loss. Liver function was abnormal with mildly raised alkaline phosphatase and aspartate transaminase. Liver biopsy and colonic biopsy showed a granulomatous vasculitis, involving both arteries and veins. She had no history of food intolerance or allergy. Initial treatment was with prednisolone and azathioprine. There was little response and cyclophosphamide was substituted for azathioprine. After five months therapy which caused a drug induced lymphocytopenia, the vasculitis had not improved, the patient's weight had dropped by a further 11 kg and she had developed severe diarrhoea with abdominal pains and rectal

bleeding. By then her condition required admission to hospital.

On admission she was taking prednisolone (ec) 10 and 15 mg on alternate days, cyclophosphamide 100 mg once a day, spironolactone 50 mg twice a day and cimetidine 400 mg twice a day. Her weight was only 50 kg after a total weight loss of 20 kg. Clinically, her abdomen was generally distended and there was evidence of gross fluid retention: the peripheral neuropathy was unchanged. Initial investigations revealed Hb 10.7 g/dl, with a lymphocytopenia and ESR 34 mm/h. Urea, electrolytes, creatinine, calcium, phosphate, thyroid and liver function tests were normal. The serum B₁₂ concentration was low and a Schilling test showed impaired absorption of B₁₂ with and without intrinsic factor. Other tests of small intestine function showed reduced xylose absorption and increased faecal fat excretion (7.6 g/24 h over five days). A C₁₄ labelled breath test was negative.

With intravenous hydration and nasogastric suction, the abdominal pains resolved. Several attempts at refeeding, even with elemental feeds (Vivonex) failed because of recurrence of abdominal pain and diarrhoea. Her condition deteriorated further and total parenteral feeding was started.

At this stage the gastrointestinal tract was further investigated. Barium enema showed features of a pancolitis with a granular mucosa and lack of haustra-

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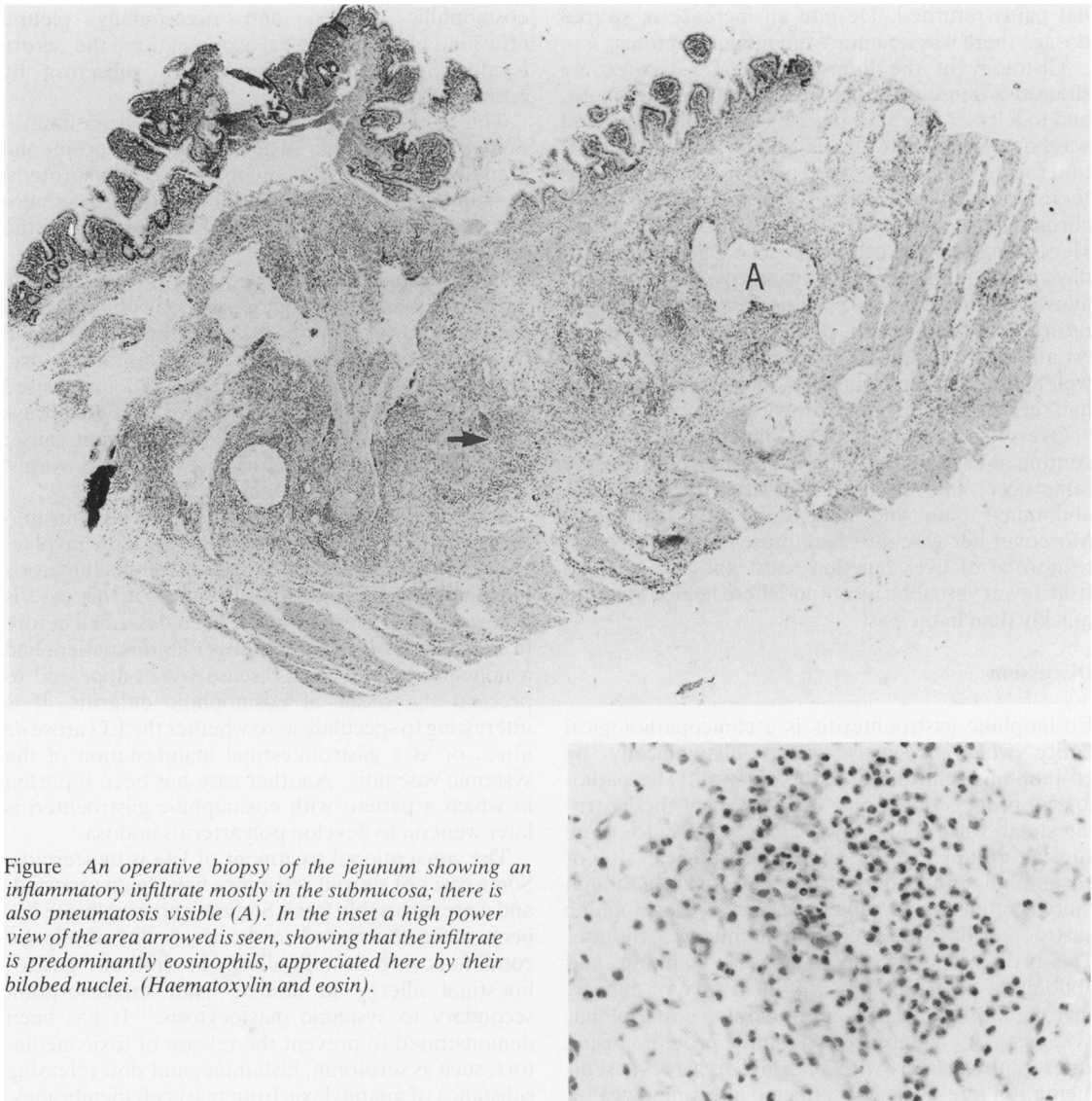


Figure An operative biopsy of the jejunum showing an inflammatory infiltrate mostly in the submucosa; there is also pneumatosis visible (A). In the inset a high power view of the area arrowed is seen, showing that the infiltrate is predominantly eosinophils, appreciated here by their bilobed nuclei. (Haematoxylin and eosin).

tions. Colonoscopies showed a granular mucosa, with areas of contact bleeding and blue pedunculated lesions that bled profusely on biopsy. Barium meal and follow through revealed dilated loops of small bowel with three apparent strictures in the proximal and mid ileum. The small bowel transit time was grossly increased (24 hours, despite metoclopramide). Atrophic and fibrotic changes were seen on histological examination of biopsies of colonic and rectal mucosae, suggesting a resolving ulceration and reactive amyloid (AA) deposits were found.

A laparotomy was done with the intention of

resecting the strictures, as the patient's condition continued to worsen. The whole of the small bowel looked distended, thickened, and abnormal. The large bowel had the appearance of a 'burnt out' colitis: although no strictures could be found, the bowel wall felt thick and rigid and it was very difficult to milk the bowel contents in either direction. Full thickness biopsies were taken. Postoperatively, she was put on a high protein, high calorie total parenteral feeding regime, during which her condition improved. When oral refeeding was started with a low fat diet, she felt unwell and the diarrhoea and abdomi-

nal pains returned. Despite an increase in steroid dosage there was no improvement in symptoms.

Histology of the biopsies taken at laparotomy showed a dense eosinophilic infiltration of mucosa, and to a lesser extent of muscle (Figure). Also found was pneumatosis intestinalis, and an amyloid infiltration (again of the 'AA' type). A diagnosis of EG was therefore established. For this reason, oral sodium chromoglycate was started at a dose of 100 mg qds. Her medication was otherwise unchanged. Within 10 days, her symptoms gradually improved and she was allowed home. Over the ensuing 10 weeks the patient returned to good health, putting on 10 kg in weight. At a follow up clinic visit two months later she was well and taking a normal diet: moreover her weight had returned to the premorbid level.

Over the next two and a half years, she has continued to take oral sodium chromoglycate in the same dose, and remained free from the diarrhoea, abdominal pain and distention suffered before. Moreover her vasculitis had improved with a return to normal of liver function tests, and she suffered from fewer vasculitic ulcers and these healed up more quickly than in the past.

Discussion

Eosinophilic gastroenteritis is a clinicopathological entity which is characterised histologically by eosinophilic infiltration of the gut wall. The pathological process may occur in any part of the gastrointestinal tract and may be classified into three clinical groups, based on the histological site of eosinophilic infiltration of the bowel wall, although there is often considerable overlap:¹ (a) Eosinophilic gastroenteritis with predominant mucosal disease. This produces symptoms of nausea, vomiting, and abdominal pain, possibly with a history of allergy. Investigation reveals peripheral eosinophilia, evidence of malabsorption, and protein losing enteropathy, usually with a normal erythrocyte sedimentation rate. Biopsy of affected intestine reveals a variable infiltration of mucosa by eosinophils. The abnormal bowel changes usually revert back to normal after treatment with corticosteroids. (b) Eosinophilic gastroenteritis with predominant involvement of the muscle layer. These patients too may have a preceeding history of allergy, food intolerance, or peripheral eosinophilia. They present with pyloric, or small bowel obstruction. Examination of affected bowel reveals macroscopically, thickening and rigidity of the wall, and microscopically, diffuse infiltration of submucosa and muscularis with sheets of eosinophils. (c) Eosinophilic gastroenteritis with predominantly serosal disease. This form is rare. There is an associated

eosinophilic ascites, and occasionally pleural effusion. On pathological examination, the serosa is thickened, with infiltration of subserosa by eosinophils.

The tissue damage probably results from infiltration by eosinophils. The toxicity of eosinophil granule proteins (especially the major basic protein) to mammalian intestine is well known both *in vitro* and *in vivo*,² and it is likely that these proteins are the mediators of tissue injury.

Unless mucosa is involved, the disease may be particularly hard to diagnose without obtaining full thickness bowel biopsies at laparotomy.^{3,4} It should be considered in patients with an appropriate history, peripheral eosinophilia, normal ESR, and raised serum IgE⁵ although not all these features are always present. In most cases there is no apparent cause; occasional causative factors are: herring worms⁶ *Trichuris trichura*,⁷ and other parasites.

It can be seen that the case presented here fits into the group EG with predominant mucosal involvement. The presence of amyloid and pneumatosis intestinalis in the intestinal biopsies of this case is noteworthy, as these have not been described before in association with EG. Moreover, as this patient had a non-specific vasculitic disease which appeared to precede the onset of eosinophilic enteritis, it is interesting to speculate as to whether the EG arose *de novo*, or as a gastrointestinal manifestation of the systemic vasculitis. Another case has been reported in which a patient with eosinophilic gastroenteritis later went on to develop polyarteritis nodosa.⁸

The conventional treatment of EG is by steroids. Some cases of steroid resistance have been reported, and were invariably fatal. Sodium chromoglycate has been successfully used in the treatment of allergic conditions such as milk allergy in children,⁹ gastrointestinal allergy in adults,¹⁰ and malabsorption secondary to systemic mastocytosis.¹¹ It has been demonstrated to prevent the release of toxic mediators, such as serotonin, histamine, and slow releasing substance of anaphylaxis from mast cell membranes. This represents a logical therapy for a possibly allergic disorder, and has been successfully used in treating EG associated with polyarteritis nodosa⁸ and in a patient who developed EG after gold therapy,¹² although clinical improvement in this case may have just been due to stopping the gold.

It is of interest that not only did the EG resolve with sodium chromoglycate therapy, but the systemic vasculitis also was far less active after this treatment. This may be supportive evidence in favour of the EG occurring as part of the systemic vasculitis: it would be most unusual for a systemic vasculitis to respond so dramatically to sodium chromoglycate after steroid and cytotoxic therapy had failed.

We believe this to be the first report of a patient who has developed EG that has not responded to either an elemental diet or to high dose steroid therapy, but has responded to sodium chromoglycate.

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